REMARKS

Claims 11 and 14-25 were pending in the present application. Claims 14-16 and 21-25 have been withdrawn from consideration.

I. The Claimed Invention Is Not Obvious

Claims 11 and 17-20 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the combination of Ortlepp et al., Eur. J. Pharmacol., 2002, 436, 145-150 (hereinafter, the "Ortlepp reference") and Yoneyama et al., Jpn. J. Pharmacol., 2002, 89, 193-196 (hereinafter, the "Yoneyama reference") in view of STN, RN 133240-46-7, 1991 (hereinafter, the "STN reference"). Applicants traverse the rejection and respectfully request reconsideration because the combination of cited references fails to produce the claimed invention.

The Office's position is that it would have been *prima facie* obvious for one skilled in the art to modify the methods described in the Ortlepp reference by substituting compound I:4 (reported in the Yoneyama reference and the STN reference) in place of irbesartan. The Office points out that both compounds are considered to be angiotensin II receptor antagonists. Applicants respectfully disagree with the Office's rejection. Indeed, the methods reported in the Ortlepp reference do not render the claimed subject matter of the present application obvious, and the addition of the Yoneyama and STN references do not cure the deficiencies of the Ortlepp reference.

As a preliminary matter, the Ortlepp reference reports a study comparing the effect of an ACE inhibitor and the effect of an angiotensin II inhibitor on hypertension, cardiac hypertrophy, hyperinsulinemia and atherosclerotic plaque in mice. In contrast, the present invention is directed to treating metabolic syndrome in a human by administering an angiotensin II type 1 receptor antagonist. Applicants will agree to amend the claims to recite "human" rather than "subject" if the Office so desires. The Ortlepp reference is, thus, irrelevant for the present invention, which regards humans.

As pointed out in Applicants' specification, metabolic syndrome is a definition made by the World Health Organization (WHO) and refers only to human beings (see, page 2, lines 7-20 of the published PCT application). The section reads:

The metabolic syndrome
The metabolic syndrome is herein defined in accordance with the definition of the World Health Organization, i.e. according to the following criteria [World Health Organization (WHO). Department of Noncommunicable Disease Surveillance. Geneva: WHO 1999 pp 1-59]:

1. Fasting plasma glucose above 6.1 mmol/L

2. Blood pressure above 140/90 mm Hg

3. One or more of the following:

    a) Plasma triglycerides above 1.7 mmol/L and/or HDL below 0.9 mmol/L (men), below 1.0 mmol/L (women)

    b) Body mass index above 30 kg/m2

All these parameters refer to humans. It is, therefore, incorrect to state that the mice in the Ortlepp reference suffered from metabolic syndrome. For example, one of the parameters for being diagnosed as having metabolic syndrome is having a body mass index above 30. To calculate body mass index, the weight of the patient, in kilograms, is divided with the length of the patient multiplied by itself, measured in meters. Obviously, body mass index in the WHO definition of the metabolic syndrome, does not apply to mice.

Further, there is no baseline given in the Ortlepp reference for plasma triglycerides. For placebo, it is given at a level lower than the definition of a human diagnosed with metabolic syndrome would have. There is no teaching or suggestion in the Ortlepp reference of what the threshold would have been, would there have been a definition for metabolic syndrome in mice.

Yet another parameter for diagnosing a human as having metabolic syndrome is a blood pressure over 140/90 mmHg. The baseline for the mice in the study disclosed in the Ortlepp reference is about 110/73.

The mice participating in the study reported in the Ortlepp reference would not have fulfilled the parameters to be diagnosed with having the metabolic syndrome, had they been humans. Indeed, the mice of the Ortlepp reference did not have metabolic syndrome according to the WHO definition. They did not even have high blood pressure according to the definition. Thus, the Ortlepp reference does not disclose the treatment of the metabolic syndrome as defined

in the specification, i.e. humans fulfilling the WHO parameters above. Given these facts, a person skilled in the art would not draw any conclusions as to the usefulness of angiotensin II inhibitors for treating metabolic syndrome. Neither one of the Yoneyama or STN references cures the deficiencies of the Ortlepp reference.

Thus, the claimed invention is not obvious in view of the combination of cited references. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

II. Conclusion

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Office is invited to contact Applicants' undersigned representative at 610.640.7859 if there are any questions regarding Applicants' claimed invention.

The Commissioner is hereby authorized to debit any underpayment of fee due or credit any overpayment to Deposit Account No. 50-0436.

Respectfully submitted,

/Paul K. Legaard, Reg.# 38534/
Paul K. Legaard, Ph.D.

Date: **9 September 2009**

Pepper Hamilton LLP
400 Berwyn Park
899 Cassatt Road
Berwyn, PA 19312-1183

Telephone: 610.640.7859
Facsimile: 267.430.7647